510(k) Substantial Equivalence Determination
Decision Summary

SEP 13 2012

A. 510(k) number: K122019

B. Purpose for Submission:

To determine substantial equivalence for the ***illumigene®*** Group A *Streptococcus* (Group A Strep) DNA Amplification Assay used for the qualitative detection of *Streptococcus pyogenes*.

C. Measurand:

Segment of the *Streptococcus pyogenes* genome

D. Type of Test:

Qualitative in vitro diagnostic using Loop-mediated isothermal DNA amplification (LAMP) technology

E. Applicant:

Meridian Bioscience, Inc. 3471 River Hills Drive, Cincinnati, OH 45244 USA

F. Propriety and Established Names:

illumigene® Group A *Streptococcus* (Group A Strep) DNA Amplification Assay
illumigene® Group A *Streptococcus* (Group A Strep) External Control Kit

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
OYZ, Group A *Streptococcus* Nucleic Acid Amplification Assay System	Class I	21 CFR § 866.3740	Microbiology (83)

H. Intended Use:

1. Intended use(s):

The ***illumigene®*** Group A *Streptococcus* (Group A Strep) assay, performed on the ***illumipro-10™***, is a qualitative in vitro diagnostic test for the detection of *Streptococcus pyogenes* (Group A β-hemolytic *Streptococcus*) in throat swab specimens.

The ***illumigene*** Group A Strep assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Streptococcus pyogenes* by targeting a segment of the *Streptococcus pyogenes* genome. Results from the ***illumigene*** Group A Strep assay can be used as an aid in the diagnosis of Group A Streptococcal pharyngitis. The assay is not intended to monitor treatment for Group A *Streptococcus* infections.

illumigene Group A Strep is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

2. Indication(s) for use:

The ***illumigene***® Group A *Streptococcus* (Group A Strep) assay, performed on the ***illumipro-10***™, is a qualitative in vitro diagnostic test for the detection of *Streptococcus pyogenes* (Group A β-hemolytic *Streptococcus*) in throat swab specimens.

The ***illumigene*** Group A Strep assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Streptococcus pyogenes* by targeting a segment of the *Streptococcus pyogenes* genome. Results from the ***illumigene*** Group A Strep assay can be used as an aid in the diagnosis of Group A Streptococcal pharyngitis. The assay is not intended to monitor treatment for Group A *Streptococcus* infections.

illumigene Group A Strep is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

3. Special Conditions for use statement(s):

- For Prescription Use Only
- The device is not intended for point-of-care use

4. Special instrument requirements:

illumipro-10™ Automated Isothermal Amplification and Detection System

I. Device Description:

The ***illumigene*** Molecular Diagnostic Test System is comprised of the ***illumigene***® Group A Group A Strep DNA Amplification Test Kit, the ***illumigene***® Group A Strep External Control Kit and the ***illumipro-10***™ Automated Isothermal Amplification and Detection System.

The ***illumigene*** Group A Strep assay utilizes loop-mediated isothermal amplification (LAMP) technology to detect the presence of *Streptococcus pyogenes* (Group A beta-hemolytic *Streptococcus*) in throat swab specimens. Each ***illumigene*** Group A Strep assay is completed using an ***illumigene*** Sample Preparation Apparatus II/Negative Control III containing Control material, an ***illumigene*** Group A *Streptococcus* Test Device and an ***illumigene*** Heat Treatment Tube. Samples are diluted in the ***illumigene*** Sample Preparation Apparatus II and dispensed into an ***illumigene*** Heat Treatment Tube. Target and Control DNA is made available for isothermal amplification via heat-treatment. DNA amplification occurs in the ***illumigene*** Test Device.

The ***illumipro-10*** heats each ***illumigene*** Group A Strep Test Device containing prepared sample and Control material, facilitating amplification of target DNA. When *S. pyogenes* is present in the throat swab specimen, a 206 base pair sequence of the *S. pyogenes* genome is amplified and magnesium pyrophosphate is generated. Magnesium pyrophosphate forms a precipitate in the reaction mixture. The ***illumipro-10*** monitors the absorbance characteristics of the reaction solutions at the assay Run Start ($Signal_{initial}$, S_i) and at the assay Run End ($Signal_{final}$, S_f). The ***illumipro-10*** calculates the change in light transmission between Run End and Run Start (S_f:S_i) and compares the ratio to a fixed cut-off value for disposition of results.

Fixed cut-off values for the TEST chamber are used to report sample results. TEST chamber S_f:S_i ratios less than 82% are reported as 'POSITIVE'; TEST chamber S_f:S_i ratios greater than or equal to 82% are reported as 'NEGATIVE'. *Numerical values are not reported.* Fixed cut-off values for the CONTROL chamber are used to determine validity. CONTROL chamber S_f:S_i ratios less than 90% are considered valid and allow for reporting of TEST chamber results

(POSITIVE, NEGATIVE). CONTROL chamber S_f:S_i ratios greater than or equal to 90% are considered invalid and prevent reporting of TEST chamber results. Invalid CONTROL chamber reactions are reported as 'INVALID'. *Numerical values are not reported.* More stringent cut-off criteria are applied to the CONTROL chamber reaction to ensure amplification is not inhibited, reagents are performing as intended and that sample processing was performed appropriately.

The ***illumigene*** Group A Strep External Control Kit contains a Positive Control Reagent. The External Positive control Reagent is used in conjunction with the ***illumigene*** Sample Preparation Apparatus II/Negative Control III reagent included in the ***illumigene*** Group A Strep Kit as part of routine Quality Control testing. External Control reagents are provided to aid the user in detection of reagent deterioration, adverse environmental or test conditions, or variance in operator performance that may lead to test errors.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   GEN-PROBE® Group A *Streptococcus* Direct Test; Catalog 103890
2. Predicate 510(k) numbers:
   K924715
3. Comparison with predicates:

Similarities		
Item	**DEVICE** ***illumigene*® Group A *Streptococcus***	**PREDICATE** **GEN-PROBE® Group A *Streptococcus* Direct** **K924715**
Intended Use	Qualitative	Qualitative
Test Format	Molecular-based Amplification Assay	Molecular-based Direct Assay
Target	*Streptococcus pyogenes*	*Streptococcus pyogenes*
Specimen Types	Throat Swab	Throat Swab
Detection	Self contained and automated	Self contained and automated

Differences		
Item	**DEVICE** *illumigene*® **Group A** *Streptococcus*	**PREDICATE** **GEN-PROBE® Group A** *Streptococcus* **Direct K924715**
Test Format	DNA Amplification Assay; Loop-Mediated Isothermal Amplification (LAMP)	Nucleic Acid Hybridization
Target Sequences Detected	206 base pair (bp) sequence *S. pyogenes* genome, resident in the pyrogenic exotoxin B (speB) gene	*Streptococcus pyogenes* ribosomal RNA
Reagents/Components	• *illumigene* Sample Preparation Apparatus II/Negative Control III • *illumigene* Group A *Streptococcus* Test Device • *illumigene* Heat Treatment Tubes	• Lysis Reagent • Probe Reagent • Hybridization Buffer • Selection Reagent • Positive Control • Negative Control • Sealing Cards • Polypropylene Tubes
Amplification	Self contained and automated	Not Appliable
Testing Time	Less than 60 minutes	Less than 90 minutes
Instrumentation	*illumipro-10™* Automated Isothermal Amplification and Detection System	GEN-PROBE® LEADER® Luminometer
Reading Method	Visible Light Transmission	Chemiluminescent Emissions
Performance Characteristics	**Sensitivity: 98.0%** [95% CI: 93.1% - 99.5%] **Specificity: 97.7%** [95% CI: 96.3% - 98.6%]	**Sensitivity: 94.1%** **Specificity: 98.3%**

K. Standard/Guidance Document Referenced (if applicable):

- Clinical and Laboratory Standards Institute. 2008. User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline- Second Edition (EP12-A)
- Clinical and Laboratory Standards Institute. 2005. User Verification of Performance for Precision and Trueness; Approved Guideline- Second Edition (EP15-A2)
- Clinical and Laboratory Standards Institute. 2005. Interference Testing in Clinical Chemistry; Approved Guideline- Second Edition (EP7-A2)

L. Test Principle:

The *illumigene* Group A Strep assay is based on loop-mediated isothermal amplification technology (LAMP). Loop-mediated amplification of DNA is accomplished by the use of specially designed primers that provide specific and continuous isothermal amplification. Magnesium-pyrophosphate is produced as a by-product of LAMP amplification. The magnesium-pyrophosphate forms a white precipitate in the reaction solution, giving the reaction solution a turbid appearance. Change in sample absorbance created by precipitation of magnesium pyrophosphate indicates the presence of target DNA and is considered a positive reaction. The absence of target DNA results in no significant change in sample absorbance and is considered a negative reaction.

M. Performance Characteristics (if/when applicable):

1. Analytical Performance:

a. Precision/Reproducibility:

Blind-coded panels of 10 samples were supplied to three independent laboratories. Samples were randomly sorted within each panel to mask sample identities. The panels included contrived samples manufactured as low positive samples (i.e. limit of detection, n = 3) and high negative samples (n = 3). The panels also included contrived positive (n = 3) samples and natural negative samples (n = 1). Testing was performed by different operators at each site on the same day (intra-assay variability) for five days (inter-assay variability). Three lots of ***illumigene*** Group A Strep and five ***illumipro-10*** instruments were used in this study. The results are given in the table below:

	Site 1		Site 2		Site 3		Total	
Sample Type	**Percent agreement**		**Percent agreement**		**Percent agreement**		**Percent agreement**	
Negative	10/10	100%	10/10	100%	10/10	100%	30/30	100%
High Negative	29/30	96.7%	30/30	100%	28/30	93.3%	87/90	96.7%
Low Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%
Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%

b. Linearity/assay reportable range:

Not applicable as this assay is qualitative

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Stability:
Sample storage and hold time studies were performed to characterize ***illumigene*** Group A Strep assay ranges. Validation studies performed at Meridian were completed using rayon swabs in both Liquid Amies (without charcoal) and Liquid Stuart Transport Medium.

Study results demonstrated that throat swab samples can be held at 21-27 C for up to 48 hours or at 2-8 C for up to 7 days prior to testing. Samples diluted in the ***illumigene*** Sample Preparation Apparatus can be held at 2-29 C for up to 2 hours prior to heat treatment. Heat-treated samples may be held at 21-29 C for up to one hour prior to testing.

Final testing demonstrated that rayon, polyester and flocked nylon swab types with either Liquid Amies (without charcoal) or Liquid Stuart Transport Medium perform acceptably with the ***illumigene*** Group A Strep assay. Swab and transport medium types with demonstrated performance in the ***illumigene*** Group A Strep assay appear in the Package Insert.

d. Detection limit:

Sensitivity studies were designed to determine the analytical limit of detection of *S. pyogenes* in throat swab specimens. Two common strains of *S. pyogenes,* ATCC 12344 and ATCC 19615, were evaluated with the ***illumigene*** Group A Strep assay. Each strain was spiked into sterile saline and

diluted serially. Dilutions were combined with negative matrix (rayon swabs inoculated with normal throat flora screened negative for *S. pyogenes,* and Liquid Amies (without charcoal) Transport Media) prior to testing. A minimum of twenty replicates for each dilution were individually processed and tested to establish limit of detect. Testing was performed using three production lots of ***illumigene*** Group A Strep and six ***illumipro-10*** instruments. External Positive and Negative Controls were tested each day throughout the study. The Limit of Detection for the assay was reported as 400 CFU/Test for ATCC 12344 and 430 CFU/Test for ATCC 19615.

The following *S. pyogenes* strains were tested and produced positive reactions at or below stated assay limit of detect of 400 CFU/Test with ***illumigene*** Group A Strep: ATCC 12384, NCIMB 13285, CCUG 33061, CCUG 33409, CCUG 39158, ATCC 49399, CCUG 53553.

Limit of Detection studies are acceptable.

e. *Analytical specificity:*

Interference Testing:

Interfering substance testing was performed to assess the potential impact of non-microbial contaminants expected to be present in throat swab samples on ***illumigene*** Group A Strep test results. Potentially interfering substances were tested with negative and contrived positive (ATCC 12344, ATCC 19615) samples. Contrived positive samples were prepared near the reported limit of detection for each strain tested. Negative samples and contrived positive samples were added to the ***illumigene*** Sample Preparation Apparatus II and inoculated with throat swab matrix (rayon swab inoculated with normal throat flora, screened negative for *Streptococcus pyogenes,* and Liquid Amies Transport Medium). Each inoculated sample was tested in triplicate.

The following biological substances, at the saturated solvent/diluent concentrations indicated, do not interfere with test results: Mucus (5.0mg/mL), Human saliva (10% v/v), and Whole Blood (2.5% v/v). Whole Blood at concentrations greater than 2.5% v/v may interfere with the ***illumigene*** Group A Strep Assay.

The following chemical substances, at the saturated solvent/diluents concentrations indicated, do not interfere with test results: Acetaminophen (19.5 mg/mL), Aspirin (12.3 mg/mL), Cepacol® Mouthwash, [Cetyopridinium Chloride (0.005% v/v)], Cepacol® Sore Throat Lozenges [Benzocaine (0.09 mg/mL), Menthol (0.02 mg/mL)], Chloraseptic® Oral Anesthetic/Analgesic [Phenol (0.07% v/v)], Contac® Cold + Flu Tablets [Acetaminophen (16.2 mg/mL), Chlorpheniramine maleate (0.06 mg/mL), Phenylephrine HCl (0.16 mg/mL)], Crest® Complete Toothpaste [Sodium fluoride (0.1 mg/mL)], Diphenhydramine HCl (2.7 mg/mL), HALLS® Cough Drops [Menthol (0.08 mg/mL)], Ibuprofen (15.6 mg/mL), Listerine® Antiseptic Mouthwash [Eucalyptol (0.0092% v/v), Menthol (0.0042% v/v), Methyl salicylate (0.0060% v/v), Thymol (0.0064% v/v)], Robitussin® Cough/Chest Congestion Cough Syrup [Dextromethorphan HBr (0.2 mg/mL), Guaifenesin (2.0 mg/mL)].

Zicam® Oral Mist [Zincum Aceticum 2X, Zincum Gluonicum 1X (0.625% v/v) produced invalid results in all replicates tested.

Interference studies are acceptable.

Cross-Reactivity Study:

Potentially cross-reacting microorganisms expected to be present in throat swab specimens were added to negative and contrived positive samples. The negative sample was prepared from *S. pyogenes* negative clinical throat swab sample in Liquid Amies (without charcoal) Transport Medium. The contrived positive sample was prepared by spiking sterile saline with *Streptococcus pyogenes,* strain ATCC 12344 at approximately 400 CFU/Test, the reported limit of detection for the strain.

Potentially cross-reactive microorganisms were added at concentrations of 1.2×10^8 CFU/mL (bacteria and fungi); Human DNA was tested at 0.02 mg/mL. Dilution controls for each sample were prepared by adding sterile saline solution in place of the potentially cross-reactive microorganisms. Each sample was tested in triplicate. No microorganism tested met the definition of interferent or cross-reactive.

None of the following organisms reacted with ***illumigene*** Group A Strep: *Acinetobacter baumannii, Acinetobacter lwoffii, Aeromonas hydrophila, Arcanobacterium haemolyticum, Bordetella bronchiseptica, Bordetella holmesii, Bordetella parapertussis, Bordetella pertussis, Burkholderia cepacia, Campylobacter jejuni, Candida albicans, Citrobacter freundii, Corynebacterium diphtheria, Corynebacterium pseudodiphtheriticum, Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Haemophilus influenza, Klebsiella oxytoca, Klebsiella pneumoniae, Lactococcus lactis, Legionella jordanis, Legionella micdadei, Legionella pneumophila, Listeria monocytogenes, Moraxella catarrhalis, Morganella morganii, Neisseria gonorrhoeae, Neisseria meningitidis, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Pseudomonas fluorescens, Staphylococcus aureus, Staphylococcus epidermidis, Stenotrophomonas maltophilia, Streptococcus agalactiae, Streptococcus anginosus, Streptococcus bovis, Streptococcus canis, Streptococcus dysgalactiae (subspecies equisimilis), Streptococcus equinus, Streptococcus intermedius, Streptococcus mitis, Streptococcus mutans, Streptococcus pneumoniae, Streptococcus salivarius, Streptococcus suis, Streptococcus uberis, Streptococcus sp. Viridans* type.

Mycoplasma pneumoniae was tested at 1.5×10^6 CFU/mL with no reaction with the ***illumigene*** Group A Strep assay.

Cross-reactivity studies are acceptable.

f. Assay cut-off:

The ***illumigene*** Group A Strep assay has a fixed cut-off based on the measured change in light transmission at the assay endpoint. The ***illumipro-10*** measures transmission of light through the Test and the Control reactions at the start of the Assay Run ($Signal_{initial}$) and at the end of the Assay Run ($Signal_{final}$). The ***illumipro-10*** calculates the change in transmission between the $Signal_{final}$:$Signal_{initial}$ and compares the result to a fixed cut-off value. Test results are reported as Positive or Negative based on comparison to the assay cut-off. Fixed cut-off values were based on well characterized clinical specimens.

2. Comparison Studies:

   a. *Method comparison with predicate device:*

      Not applicable

   b. *Matrix comparison:*

      Not applicable

3. Clinical Studies:

   a. *Clinical Sensitivity:*

      Clinical trials for the ***illumigene*** Group A *Streptococcus* (Group A Strep) DNA Amplification Assay, including the ***illumipro-10*** Automated Isothermal amplification and detection system, were conducted from April to June 2012. Performance characteristics of the assay were determined by comparison to composite bacterial culture method for Group A *Streptococcus*. A total of 798 qualified specimens were evaluated with the test; two specimens produced initial invalid results which were negative upon retest. Overall assay Sensitivity was reported as 98.0% [95% CI: 93.1 – 99.5%]; overall assay Specificity was reported as 97.7% [95% CI: 96.3 – 98.6%]; overall assay Invalid Rate was 0.3% [95% CI: 0.1 – 0.9%]. Compiled clinical study information is described below:

Table 1: *illumigene* Group A Strep Performance Data Summary

Group A *Streptococcus* Composite Culture	*illumigene* Group A Strep		
	Positive	**Negative**	**Total**
Positive	100	2	102
Negative	16	680*	696
Total	116	682	798
			95% CI
Sensitivity	100/102	**98.0%**	93.1 – 99.5%
Specificity	680/696	**97.7%**	96.3 – 98.6%
Invalid Rate	2/800	**0.3%**	0.1 – 0.9%

* Two specimens produced initial invalid results that were negative upon re-test. A total of 798 qualified specimens were evaluated with the test device and composite bacterial culture methods.

Three independent clinical test sites located in the Midwestern and Southern regions of the United States participated in the device evaluation. All samples utilized in the study were leftover human specimens, not individually identifiable. All samples included in the study were submitted to the testing laboratory by an ordering physician for Group A *Streptococcus* testing and were presumed from symptomatic patients. No restrictions were placed on age, gender, medications or known pharmaceutical therapies.

Composite culture methods were employed to accommodate reports that Group A *Streptococcus* culture is considered 90 - 95% sensitive when correct sampling and plating techniques are used. [1,2] The Composite Culture Method consisted of the Clinical Site Culture Method as performed in standard of care testing and a Reference Culture Method performed by

Meridian Bioscience. Site culture testing was performed by direct plating of the throat swab specimen while reference culture testing was performed by plating the swab transport media. Specimens producing positive Group A *Streptococcus* results from either the Site Culture Method or the Reference Culture Method were considered positive.

Specimens that generated invalid results were further evaluated. Data review for the two initial invalid samples revealed one Control Chamber failure and one suspect Test Chamber reaction. Repeat testing for both specimens produced valid, negative results. Site performance information was analyzed by Composite Culture Reference Testing and Site Culture Methods. Site performance as compared to Composite Culture Method, is summarized in Table 2. Site performance as compared to Site Culture Methods is presented in Table 3.

Table 2: *illumigene* Group A Strep Assay Performance by Site; Composite Culture Method

Site Identification	Positive Specimens			Negative Specimens			Invalid Specimens	
	illumigene /Composite Culture	% Sensitivity	95% CI	*illumigene* /Composite Culture	% Specificity	95% CI	Invalid /Total	% Invalid
Total	**100/102**	**98.0%**	**93.1 - 99.5%**	**680/696**	**97.7%**	**96.3 - 98.6%**	**2/800**	**0.3%**
Site 1	47/47	100.0%	92.4 - 100.0%	287/291	98.6%	96.5 - 99.5%	0/338	0.0%
Site 2	28/30	93.3%	78.7 - 98.2%	204/212	96.2%	92.7 - 98.1%	1/243	0.4%
Site 3	25/25	100.0%	86.7 - 100.0%	189/193	97.9%	94.8 - 99.2%	1/219	0.5%

Table 3: *illumigene* Group A Strep Assay Performance by Site; Clinical Site Culture Method

Site Identification	Positive Specimens			Negative Specimens			Invalid Specimens	
	illumigene /Composite Culture	% Sensitivity	95% CI	*illumigene* /Composite Culture	% Specificity	95% CI	Invalid /Total	% Invalid
Total	**74/74**	**100.0%**	**95.1 - 100.0%**	**682/724**	**94.2%**	**92.3 - 95.7%**	**2/800**	**0.3%**
Site 1	40/40	100.0%	91.2 - 100.0%	287/298	96.3%	93.5 - 97.9%	0/338	0.0%
Site 2	18/18	100.0%	82.4 - 100.0%	206/224	92.0%	87.7 - 94.9%	1/243	0.4%
Site 3	16/16	100.0%	80.6 - 100.0%	189/202	93.6%	89.3 - 96.2%	1/219	0.5%

Seven of the 102 Composite Culture-positive specimens were positive by Site Culture methods only; 26 of the 102 Composite Culture-positive specimens were positive only by the Reference Culture method; the two ***illumigene*** false-negative results were positive only by the Reference Culture performed by Meridian Bioscience. Statistical analysis of Site performance data was performed with no significant difference among Sites identified.

Clinical performance data was evaluated by patient age and gender. Seventy two (9.0%) patients tested were two years of age or younger; 385 (48.2%) patients were between two and 12 years of age; while 259 (32.5%) patients were greater than 12 and less than 21 years of age. The remaining 82 (10.3%) study patients were greater than 21 years old. Age information was known for all patients included in the performance analysis. No performance differences were noted based on chronological age. The study population included 410 (51.4%) female patients and 386

(48.4%) male patients. Gender was unknown for two (0.2%) of the study participants. No performance differences were noted based on gender.

References:

1. *Diagnosis and Tretament of Streptococcal Phayrngitis.* Beth A. Choby, MD. Volume 79, Number 5. March 1, 2009, American Family Physician, pp. 383-390.

2. Pediatrics, American Academy of. Group A Streptococcal Infections. Pickering LK. *Red Book: 2012 Report of the Committee on Infectious Diseases.* Elk Grove Village, IL : American Academy of Pediatrics, 29th ed., 2012, pp. 669-680.

b. Clinical Specificity:

See Section 3a

c. Other Clinical Supportive Data

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Overall incidence of *Streptococcus pyogenes* in patients tested during the 2012 clinical study was 14.6% (116/796).

N. Other Supportive Device and Instrument Information:

Instrument: ***illumipro-10™***

O. System Descriptions:

System Description was reviewed in previous submission, K100818, K110012, K112125 and K121044. No system or software changes were made for the ***illumigene*** Group A *Streptococcus* assay.

1. Modes of Operation:

The ***illumipro-10™*** heats each ***illumigene*** Group A Strep Test Device containing prepared samples and Control Reagent, facilitating amplification of target DNA. When *S. pyogenes* is present in the throat swab sample, a conserved sequence of the *S. pyogenes* is amplified and magnesium pyrophosphate is generated. Magnesium pyrophosphate forms a precipitate in the reaction mixture. The ***illumipro-10*** detects the change in light transmission through the reaction mixture created by the precipitating magnesium pyrophosphate. Sample results are reported as Positive or Negative based on the detected change in light transmission.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes_____X_____ No_____

3. Specimen Identification:

The ***illumipro-10*** utilizes software to automate incubation and detection of ***illumigene*** Molecular Diagnostic in vitro diagnostic test reactions. The ***illumipro-10*** reports sample results as INVALID, POSITIVE or NEGATIVE.

4. Specimen Sampling and Handling:

Specimens are prepared manually. Incubation and detection are automated using the ***illumipro-10***.

5. Calibration:

Calibration of the ***illumipro-10*** is not required.

6. Quality Control:

The ***illumigene*** Group A Strep External Control Kit includes a Positive Control Reagent. The External Positive Control is used in conjunction with the ***illumigene*** Sample Preparation Apparatus II/Negative Control III provided in the ***illumigene*** Group A Strep DNA Amplification Assay. External Control reagents are provided to aid the user in detection of reagent deterioration, adverse environmental or test conditions, or variance in operator performance that may lead to test errors. The ***illumigene***® Group A Strep External Control Kit is required for routine Quality Control.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

SEP 13 2012

Meridian Biosciences, Inc.
c/o Michelle L. Smith
3471 River Hills Drive
Cincinnati, OH, 45244, US

Re: k122019
Trade Name: *illumigene*® Group A Streptococcus (Group A Strep) DNA Amplification Assay
illumigene® Group A Streptococcus (Group A Strep) External Control Kit
Regulation Number: 21 CFR §866.3740
Regulation Name: Group A *Streptococcus spp.* Nucleic Acid Amplification Assay
Regulatory Class: Class I
Product Codes: OYZ, OOI
Dated: September 10, 2012
Received: September 11, 2012

Dear Ms. Smith

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

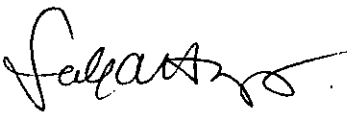
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication(s) for Use Form

510(k) Number: K122019

Device Name: ***illumigene***® Group A *Streptococcus* (Group A Strep) DNA Amplification Assay

Indications for Use:

The ***illumigene***® Group A *Streptococcus* (Group A Strep) assay, performed on the *illumipro-10*™, is a qualitative in vitro diagnostic test for the detection of *Streptococcus pyogenes* (Group A β-hemolytic *Streptococcus*) in throat swab specimens.

The *illumigene* Group A Strep assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Streptococcus pyogenes* by targeting a segment of the *Streptococcus pyogenes* genome. Results from the *illumigene* Group A Strep assay can be used as an aid in the diagnosis of Group A Streptococcal pharyngitis. The assay is not intended to monitor treatment for Group A *Streptococcus* infections.

illumigene Group A Strep is intended for use in hospital, reference or state laboratory settings. The device is not intended for point of-care use.

Prescription Use ___X___ Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) AND/OR (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K122019